

## CASE REPORT

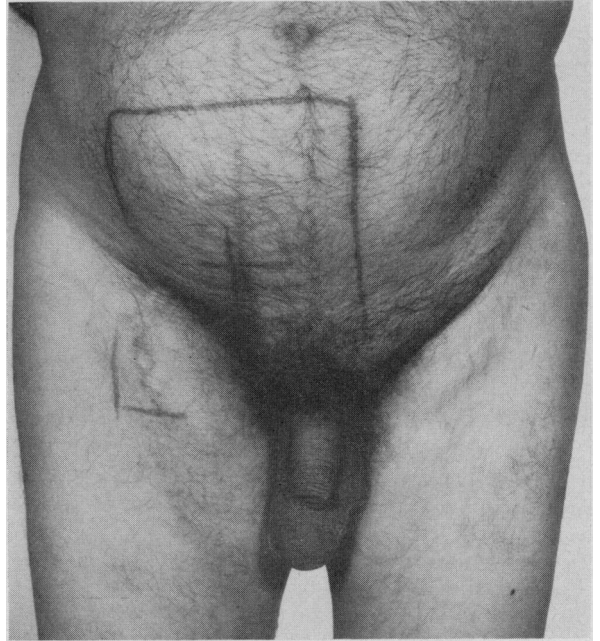
### Angiofollicular Lymph Node Hyperplasia

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**A** BETTER understanding of histological appearances has led to the reclassification of many tumours, and nowhere has this been more manifest than in the lymphomas. The correlation of histological appearance with the clinical course has identified some previously unrecognized diseases. Castleman in 1954 first drew attention to a rare form of lymph node hyperplasia occurring in the mediastinum.<sup>1</sup> Since then, some 62 cases of angiofollicular lymph node hyperplasia have been reported, situated intrathoracically in all but six patients.<sup>2-5</sup> Of the latter, one occurred in the supraclavicular fossa, two in muscle, one in the soft tissues of the shoulder and two in the retroperitoneum. The intrathoracic cases had been diagnosed mainly as thymoma and were discovered as asymptomatic masses on routine chest radiograph, although some patients had complained of cough and aching in the chest. There was frequently a long history, and in one patient described by Cates and Robinson<sup>5</sup> the condition was present for 20 years before the diagnosis was established.

The diagnosis of the first case reported in this presentation led to a search of our records, with the production of only one other case which can be placed in this category. This second case was identified among nine lymphoid tumours which did not fit into our classification for this group of diseases. Fifteen thymomas were reviewed and the diagnosis was substantiated. These cases are reported because of their rarity and unusual features, since both had a long history and presented with abdominal masses.

**CASE 1.**—A 54-year-old Italian man was first seen at the Princess Margaret Hospital in November 1965 with a puzzling history of many years' duration. A small lump had been present in the right groin since the age of 15 years but had never bothered him. In 1959 he was seen at another hospital because the lump had started to enlarge and to cause an ache. At operation a soft, greyish-pink mass of matted nodes was found in the femoro-inguinal region, with no apparent invasion. The mass was



**Fig. 1.**—Shows irradiation field covering tumour mass producing swelling of right thigh.

excised but the abdomen was not explored. Over the next six years a lump appeared in the right lower abdominal quadrant. The patient was seen at a second hospital where a mass was found arising above the inguinal ligament and which was palpable on rectal examination. The rest of the physical examination was normal. At laparotomy a large extraperitoneal non-encapsulated mass was found. The tumour infiltrated the whole of the right side of the pelvis, with the femoral vessels traversing it. Dissection proved difficult and, because the diagnosis of lymphoma was suggested by a rapid section, the abdomen was closed. Further study inclined to the view that this represented a chronic inflammatory process rather than a malignant one, but with the diagnosis in doubt the patient received a course of chlorambucil for several months. Some regression of the tumour was described, but a static stage was reached and the patient was referred to the Princess Margaret Hospital.

His general condition was excellent and he was asymptomatic, apart from swelling of the right thigh which produced a dull ache (Fig. 1). The significant finding was a firm, mildly tender mass arising from the right side of the pelvis to a height of 12 cm. above the centre of the inguinal ligament. On rectal examination the tumour was found to be

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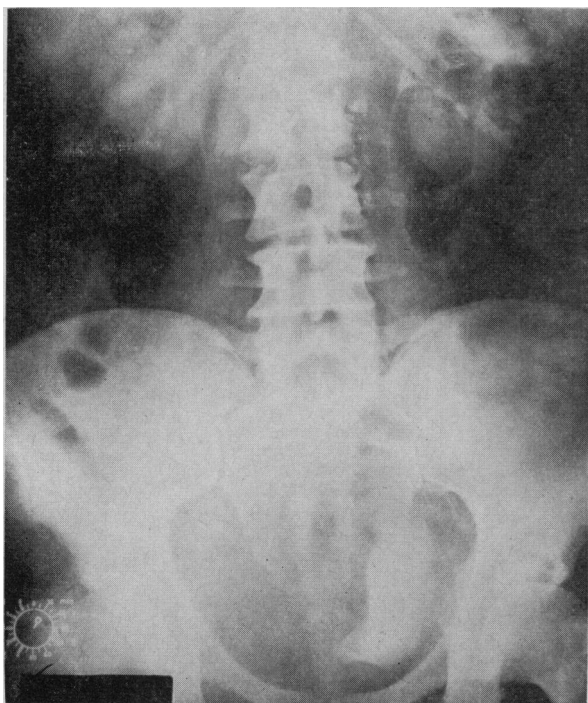


Fig. 2 (Case 1)—IVP shows filling defect in right side of bladder but with normal renal function. Lymph nodes containing contrast medium from lymphography are visible.

fixed to the pelvic wall but not to cross the midline. There was considerable edema of the right thigh but only minimal swelling of the leg. The IVP showed a large pelvic mass distorting the right side of the bladder with medial displacement of the right ureter but no evidence of hydronephrosis or urinary obstruction (Fig. 2). Lymphography showed evidence of obstruction to lymphatic flow in the region of the right groin, and the visualized lymph nodes filled normally (Fig. 3). The left lymphatic system and para-aortic nodes showed good filling and appeared normal. Blood count, sternal marrow examination, urinalysis and chest radiograph were normal.

Histological review suggested angiofollicular lymph node hyperplasia. Because of the large inoperable tumour mass producing symptoms of pain and swelling, it was elected to initiate a course of irradiation aimed at producing tumour regression with symptomatic relief. The tumour was treated with opposing fields using the Theratron 60 Cobalt unit. There was little change in the palpable mass and a tumour dose of 4500 rads was given in 34 days. Specific measurements showed the thigh swelling to remain unchanged, with a circumference 10 cm. greater at its midpoint than the left side, but the measured height of the tumour above the inguinal ligament had decreased by 2 cm. The patient has now been followed up for two years since completing irradiation, and there has been no further change in the physical signs or symptoms. This man is able to work full-time in a chicken plant, and no further therapy is planned.

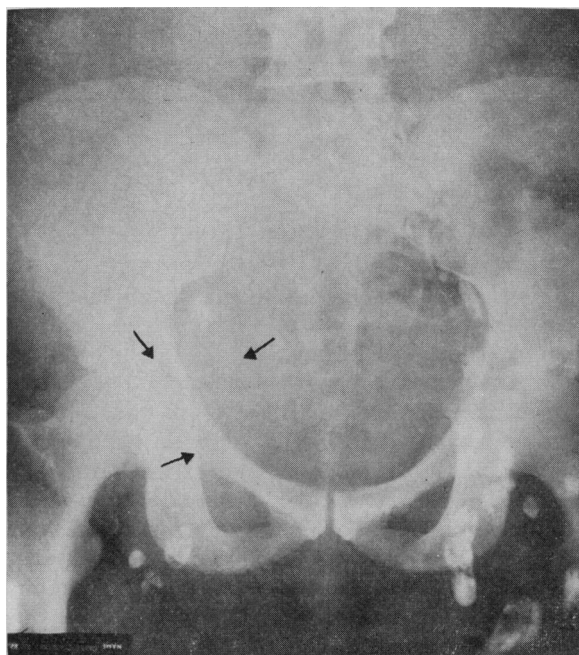


Fig. 3 (Case 1)—24-hour lymphogram. Both feet were injected and on the right side there is an area of non-filling due to obstruction of lymph flow by tumour. The left side and para-aortic nodes are normal.

**CASE 2.**—A 69-year-old English woman was first seen at the Princess Margaret Hospital in September 1962. A year previously a laparotomy had been performed at another hospital because of abdominal pain and the presence of a palpable mass in the left upper quadrant. At operation the only abnormality was a mass of lymph nodes in the small bowel mesentery, and two of these were excised. Histological examination suggested a giant follicular lymphoma progressing to diffuse lymphosarcoma. The patient received nine radiotherapy treatments, the details of which have not been traced, but the dose of radiation must have been small. Her general condition deteriorated and she was referred to the Princess Margaret Hospital for further assessment.

Clinical examination showed her to be frail and weighing only 96 lbs. Apart from chronic frontal headaches her only symptom was continuous abdominal pain centred around the umbilicus and unrelieved by any treatment. The only abnormality was diffuse central abdominal tenderness, but no masses were felt. All investigations, including blood count, bone marrow examination, urinalysis, chest radiograph, IVP and GI series, were normal. When lymphography was performed, for technical reasons only the left side filled, but all visualized nodes were normal. Because of persistent abdominal pain, an examination under anesthesia was carried out together with uterine curettage, but no abnormality was found. Pathological review showed the same histological picture as in Case 1 and the diagnosis of angiofollicular lymph node hyperplasia was made. The patient has now been followed up for six years and there is no clinical evidence of tumour. Because of persistent but vague abdominal pain, a repeat

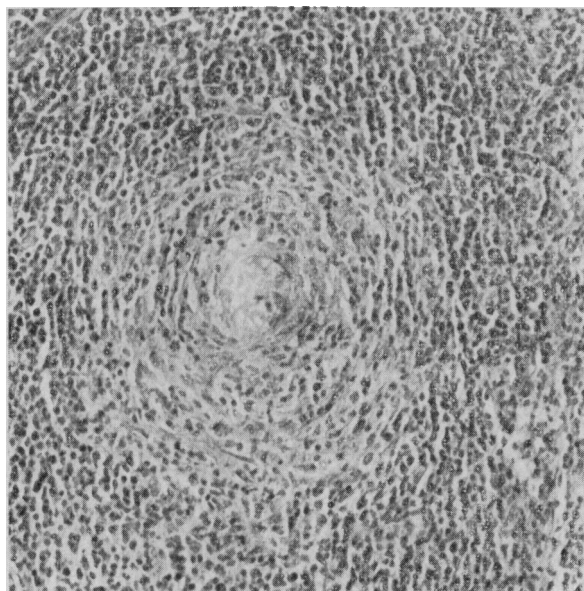


Fig. 4 (Case 1)—A follicle-like structure, situated in densely packed mature lymphocytes of the type that were diffusely distributed so that the two constituents displaced the normal structure of lymphoid tissue. (Hematoxylin and eosin,  $\times 125$ .)

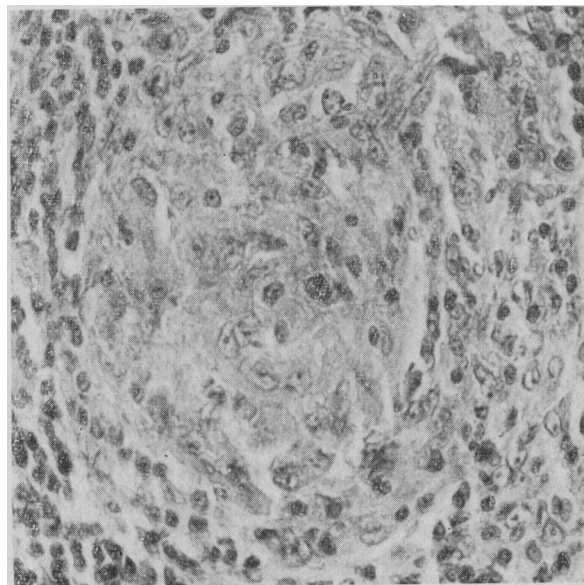


Fig. 5 (Case 1)—Swollen endothelial cells, constituting the centre of the pseudofollicle, are embedded in mature lymphocytes mixed with a small number of reticulum cells. (Hematoxylin and eosin,  $\times 500$ .)

lymphogram and GI series were done six months ago and were normal.

#### DISCUSSION

This type of tumour has been called pseudolymphoma and sometimes Castleman's lymphoma. A better name is angiofollicular lymph node hyperplasia, which describes the histological picture. The nodal architecture is abnormal, with follicles scattered throughout. The germinal centres show capillary vessels branching in the centre of masses of lymphocytes with their central areas showing hyalinization (Figs. 4 and 5). The tissue between the lymphoid follicles is composed of vascular channels with variable collagenous thickening of the walls and lined by plump endothelial cells. Lymphocytes are densely packed and diffusely distributed throughout, and fibrous trabeculae are present. Grossly, the tumours have been a single mass in most cases, but a few were composed of two or three adjacent masses looking like enlarged lymph nodes. When sectioned the tissue is smooth, soft, homogeneously grey-red and sometimes hemorrhagic.

The etiology is unknown and the tumour pursues a benign course. Castleman, Iverson and Pardo Menendez<sup>2</sup> regarded the lesion as a benign hyperplastic one, probably resulting from a low-grade, non-specific, chronic inflammatory process of several years' duration. Lattes and Pachter<sup>6</sup> described the same histological pattern in cervical, mediastinal and retroperi-

toneal lymph nodes and in soft tissue and muscle. Their view was that these lesions were examples of hamartoma. Harrison and Bernatz,<sup>3</sup> reporting their experience from the Mayo Clinic, coined the term angiofollicular lymph node hyperplasia, thereby providing the most effective descriptive term for this lesion. Zettergren<sup>7</sup> thought the tumour was a benign neoplastic one and Chipman and Dolan,<sup>8</sup> noting the vascular sclerosis, suggested that a mechanical factor was operative.

Angiofollicular lymph node hyperplasia is certainly more common than reports indicate. Our view is that the sclerosis in the vessel walls indicates a short-lived causative stimulus and that the restriction of the process to lymphoid tissue, whether nodal or extranodal, lends emphasis to the essential nature of this environment for this peculiar activity in vessels. The stimulus is probably inflammatory in nature.

The behaviour is not malignant although wide infiltration of surrounding tissues is described and was a feature of our first case. Generalized disease has not been reported nor, indeed, occurrence of the tumour in two separate anatomical areas, although multiple nodes at one site may be involved.

Lymphomatous infiltration of the skin has been called reactive pseudolymphoma, but this has very different characteristics from the tumour described.<sup>9</sup> Frequently simulating malignant lymphoma, the former condition is benign and identical with the reactive follicular hyperplasia observed in lymph nodes. Pseudolympho-

matous tumours have been reported in the gastrointestinal tract,<sup>10</sup> and these too are an expression of reactive hyperplasia.

Both of our cases had long histories. A mass was certainly present in Case 1 seven years before he was seen by us, possibly for as long as 35 years, and in Case 2 for at least six years. In Castleman's series the duration from the first appearance of symptoms to diagnosis varied from six months to eight years, and the case reported by Cates and Robinson<sup>5</sup> with a 20-year history has already been mentioned.

#### TREATMENT

The diagnosis has never been made preoperatively. Its establishment in the presence of a large mass is of paramount importance in patient management. The reported cases, all misdiagnosed at first, had excision of the tumour with excellent clinical results and without recurrence, although in several the excision was incomplete because of local infiltration. This is the treatment of choice for these benign lesions, as operation is necessary to establish the diagnosis. However, if the tumour is asymptomatic and the diagnosis is established, periodic observation is the only medical care required. Other treatment regimens have not been recorded, although one patient received postoperative irradiation and was in good health 17 years after the first appearance of symptoms and 12 years after treatment. Our first patient received moderately heavy irradiation with little change in the physi-

cal signs and no symptomatic improvement. The rationale for using radiation therapy is based on the destruction of lymphoid cells in the treatment of malignant lymphomata, with consequential disappearance of the tumour. Mature and immature lymphocytes are highly sensitive to radiation and killed by small doses of 10 to 100 rads. Radiation will also produce an obliterative endarteritis, and these two facts, with the knowledge that surgery was not possible, prompted us to advise a course of irradiation. However, there was no initial response from cellular destruction and there has been no late regression following impairment of tumour vasculature. Chemotherapy is unlikely to be effective when heavy irradiation is not, and its toxicity makes it undesirable in the treatment of benign lesions.

#### REFERENCES

1. Case Records of the Massachusetts General Hospital, Weekly Clinicopathological Exercises, Case 40011: *New Eng. J. Med.*, 250: 26, 1954.
2. CASTLEMAN, B., IVERSON, L. AND PARDO MENENDEZ, V.: *Cancer*, 9: 822, 1956.
3. HARRISON, E. G., JR. AND BERNATZ, P. E.: *Arch. Path. (Chicago)*, 75: 284, 1963.
4. TUNG, K. S. K. AND MCCORMACK, L. J.: *Cancer*, 20: 525, 1967.
5. CATES, G. W. AND ROBINSON, C. L. N.: *Canad. Med. Ass. J.*, 97: 1538, 1967.
6. LATTES, R. AND PACHTER, M. R.: *Cancer*, 15: 197, 1962.
7. ZETTERGREN, L.: *Acta Path. Microbiol. Scand.*, 51: 113, 1961.
8. CHIPMAN, C. D. AND DOLAN, F. G.: *Canad. Med. Ass. J.*, 84: 900, 1961.
9. HIRSCH, P. AND LUKES, R.: *Arch. Derm. (Chicago)*, 91: 408, 1965.
10. WEAVER, D. K. AND BATSAKIS, J. G.: *Amer. J. Gastroent.*, 44: 374, 1965.